REMARKS

Applicants have cancelled claims 2, 4 12, 19, and 20 without prejudice expressly reserving the right to pursue the subject matter of the cancelled claims in one or more subsequently filed applications.

Applicants have amended claim 1 to recite "DNA probe specific to ...." rather than "DNA probe that specifically hybridizes...."

Applicants have also amended claim 1 to recite

> "wherein the DNA sequence is present in the PBP gene of penicillin sensitive strains of *Streptococcus pneumoniae* but is modified in the PBP gene of penicillin resistant strains of *Streptococcus pneumoniae*"

and

> "wherein the DNA sequence specific to a PBP gene of penicillin resistant strains of *Streptococcus pneumoniae* is different from the DNA sequence of the PBP gene present in penicillin sensitive strains of *Streptococcus pneumoniae*"

Support for these amendments is found, e.g., on page 2, lines 4 to 16 and Figure 4.

On page 2 lines 4-6 Applicants have disclosed that a comparison of the DNA sequence of penicillin sensitive and penicillin resistant *S. pneumoniae* strains identifies regions that are present in all penicillin sensitive strains but are modified in penicillin resistant strains. Applicants have also disclosed, page 2, lines 10-16 that they developed DNA probes by which penicillin sensitive and resistant strains can be differentiated. Sequence differences between sensitive and resistant strains occur in the PBP genes and the sensitive-specific probes are selected such that they discriminate genes which code for resistant variants, i.e. are specific to sequences of sensitive strains that are not present in resistant

strains (see the sequences underlined in Fig. 4), whereas the resistant-specific probes are selected such that they hybridize with sequences modified in resistant variants, i.e. which are not present in sensitive strains.

Applicants have added claims 24-26. These claims differ from claim 1 in that "DNA probe" is replaced by "oligonucleotide." Support for claims 24-26 is found, e.g., on pages 5 and 6 of the specification and claims 1 and 8 as originally filed. Also the definition of the specificity of the sequences has been adapted in that claim 24 recites that the sensitive-specific DNA sequence is different from the resistant-specific DNA sequence aligned thereto, which language is supported by page 2 in connection with Fig. 4, which shows the differences between a sensitive gene aligned with resistant variants.

New claims 25 and 26 recite specific hybridization conditions. Support for claims 25 and 26 is found, e.g., on page 5, lines 10-15 and page 6, lines 6-8.

Claims 1 and 6 stand rejected under 35 U.S.C. §103(a) for purportedly being unpatentable over Dowson et al. in view of Kell et al. Applicants disagree and in view of the amendments to the claims and the following remarks request that the Office reconsider and withdraw the rejection of the claims.

Applicants' claimed method steps allow one to readily determine if a *Streptococcus pneumonia* isolate is a penicillin sensitive strain of *Streptococcus pneumonia* or a penicillin resistant strain of *S. pneumonia*. The special feature of the claimed method is that a sensitive-specific probe is applied in combination with a resistant-specific probe to an *S. pneumon ia* isolate, which allows an accurate determination of the isolate's resistance to penicillin. The method provides for the accurate determination even if a probe that is specific for the particular resistance gene of the assayed isolate is not used. Therefore, penicillin

resistance can be determined by Applicants' method without the necessity of using probes that are specific for every possible *S. pneumonia* resistance gene.

One of skill in the art would not have been motivated to modify the methods of Dowson and Kell as suggested by the office because the modifications would render Dowson's and Kell's methods unsatisfactory for their intended purposes.

> If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification.
>
> *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984) See MPEP Section 2143.01. V.

Dowson describes a method to study the origins of penicillin resistance in different viridians streptococci. On page 5859, 2nd column Dowson teaches screening *S. sanguis* and *S. oralis* for two gene classes of penicillin-resistant *S. pneumonia* with the probes Pn11, Pn12 and Pn13. On page 5862, last paragraph, Dowson teaches screening the streptococcal species listed in Table 1 for two resistant gene classes with probes Pn26′ and Pn29′. Hence, Dowson studies the *relatedness among different species* by screening the various different species for resistant-specific DNA sequences.

To generate the claimed method, a person of ordinary skill in the art would have had to modify Dowson's method so that the probes specific for penicillin-resistance in *S. pneumoniae* (e.g. Pn11, Pn13) and specific for penicillin-sensitive *S. pneumoniae* (e.g. Pn12) would be used *to screen the same species*, i.e. *S. pneumoniae*, rather than studying the relatedness of *different species*, e.g. *S. sanguis* or *S. oralis*.

Such a modification would render Dowson's method unsatisfactory for its intended purpose, which is to study the transfer of altered PBP genes from *S. pneumonia* into different streptococci species (see page 5858, 2nd column, 2nd paragraph). Therefore, there is no suggestion or motivation to make the proposed modification (*In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)). Thus Dowson does not render the claimed method obvious.

Moreover, the methods of Dowson and Kell would not necessarily perform the method claimed:

On page 5859, 2nd column, 3rd paragraph, Dowson reports that none of the tested oligonucleotide probes hybridized to the penicillin-sensitive strains of S. *sanguis* and *S. oralis*. What Dowson concludes is that the resistance genes are diverged between the different streptococci species. Hence, Dowson does not teach probes that are capable of discriminating between penicillin-sensitive and penicillin-resistant strains: yet such discrimination is required by Applicants' claimed method to determine whether an assayed *S. pneumonia* strain is sensitive or resistant to penicillin.

While Dowson teach screening for *specific* resistant DNA sequences in *different* viridians, this reference does not teach or suggest a method for discriminating between sensitive and resistant strains of a single species, *S. pneumoniae*. In particular, Dowson does not teach or suggest the procedure as recited in claim 1b), wherein the combination of a *S. pneumoniae* sensitive-specific probe and a *S. pneumoniae* resistant-specific probe, is used to determine whether an *S. pneumoniae* of unknown penicillin sensitivity is sensitive and resistant to penicillin.

Kell does not overcome the deficiencies of Dowson. Kell studies the relationships among resistant pneumoccocci by DNA fingerprinting and ribotyping. DNA fingerprinting is a method in which the DNA is digested by restriction enzymes and fractionated on a polyacrylamide gel (see Fig. 1).

Ribotyping is a method wherein the restriction fragments are hybridized with ribosomal RNA of *E. coli* (see page 4384, 3rd paragraph). Therefore, Kell does not teach or suggest using DNA probes specific for *S. pneumonia* PBP genes for hybridization. Kell teaches different analytical methods for studying differences among isolates known to be resistant. Therefore, Kell teaches away from the hybridization method according the method claimed.

Even if Dowson and Kell were to teach gene sequences that confer penicillin resistance, or teach screening streptococcus samples for specific resistant PBP gene variants to determine characteristics of the bacterial strains, these references do not teach or suggest discriminating between sensitive and resistant strains as recited in claim 1, step b) and to determine whether a strain is sensitive or resistant to penicillin as recited in claim 1, step c). Because Dowson and Kell in combination fail to suggest claim 1, steps b) and c), the cited art fails to render the claimed method obvious.

In view of the amendments to the claims and the foregoing remarks, Applicants request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. 103(a) in view of Dowson and Kell.

Claims 2-3 stand rejected under 35 U.S.C. §103(a) for purportedly being unpatentable over Dowson et al. in view of Kell et al. and further in view of In Re Deuel. Applicants disagree.

As discussed above, Dowson and Kell do not teach or suggest the method of claims 1 or 6. Because Kell does not teach or suggest using a probe specific for a resistant PBP gene, Kell does not suggest the use of a probe comprising SEQ ID NO:8. Even if Kell were to teach a resistant PBP gene comprising SEQ ID NO: 8, a skilled person would not have been motivated to modify Dowson to use a sensitivity-specific DNA sequence consisting of SEQ ID NO: 8 in combination with a resistant-specific DNA sequence of *S. pneumonia* to test a *Streptococcus pneumoniae* of unknown resistance for resistance to penicillin because such a

modification would have rendered the method of Dowson unsatisfactory for Dowson's intended purpose, as discussed above. Therefore, claim 3 is not obvious in view of Dowson, Kell and *In re Deuel.*

In view of the foregoing remarks and amendments to the claims, Applicants request that the Office reconsider and withdraw the rejection of the claims under 35 U.S.C. 103(a) in view of Dowson, Kell and *In Re Duell.*

Claims 1, 4, 6, 8-11, 14, 22 and 23 stand rejected under 35 U.S.C. 112, second paragraph for purportedly being indefinite. Applicants disagree.

The Office contends claims 1, 6, and 8-10 are indefinite for reciting the limitation "specifically hybridizes." Applicants disagree however the current claims do not recite the term "specifically hybridizes" and therefore request that the rejection be withdrawn as it relates to these claims.

The Office also contends that claims 4, 11, 14, 22 and 23 are indefinite for reciting the term "sequences with differ from one to four nucleotides" or "sequences which differ from one to four nucleotides under conditions that can permit hybridization." Applicants disagree, however, the current claims do not recite this phrase and as such Applicants request that the rejection as it relates to these claims be withdrawn.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket # 104049.B270037).

Respectfully submitted,

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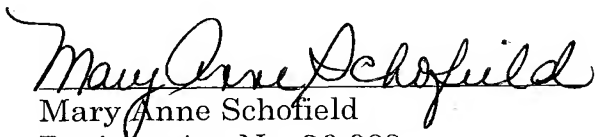

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